

the mononuclear phagocyte further comprises a binding agent capable of binding to a cell surface element of the mononuclear phagocyte.

54. (new) A mononuclear phagocyte according to claim 53 wherein the binding agent comprises a ligand adapted to bind to the cell surface element of the mononuclear phagocyte, preferably wherein the ligand is a mannosylated poly -L — lysine.

55. (new) A mononuclear phagocyte according to claim 53 wherein the binding agent comprises a viral viral for internalising the hypoxia and/or ischaemic and/or stress regulatable agent into the mononuclear phagocyte.

56. (new) A mononuclear phagocyte according to claim 51 wherein the NOI is incorporated into the genome of the mononuclear phagocyte.

57. (new) A mononuclear phagocyte according to claim 55 wherein the viral vector is a lentiviral vector.

58. (new) A mononuclear phagocyte according to claim 56 wherein the viral vector is a lentiviral vector.

59. (new) A mononuclear phagocyte according to claim 55 wherein the viral vector is an adenoviral vector.

60. (new) A mononuclear phagocyte according to claim 51 wherein at least one NOI encodes a pro-drug activation enzyme, preferably a p450 enzyme, preferably a CYP2B6 p4.50 enzyme.

61. (new) A mononuclear phagocyte according to claim 51 wherein the

62. (new) A mononuclear phagocyte according to claim 51 wherein the

62. (new) A mononuclear phagocyte according to claim 51, wherein the hypoxia and/or ischaemic and/or stress regulatable element comprises a hypoxic response element (HRE).

63. (new) A mononuclear phagocyte according to claim 51 wherein the hypoxia and/or ischaemic and/or stress regulatable element comprises an inducible or repressible promoter element.

64. (new) A mononuclear phagocyte according to claim 63 wherein the inducible or repressible promoter element comprises a tetracycline repressor DNA sequence.

65. (new) A mononuclear phagocyte according to claim 51 wherein the mononuclear phagocyte further comprises an NOI encoding an activating or control product.

66. (new) A mononuclear phagocyte according to claim 65 wherein the activating product is HIF1-alpha.

67. (new) A mononuclear phagocyte according to claim 65 wherein the control product is a tetracycline repressor protein.

68. (new) A mononuclear phagocyte according to claim 51 wherein there is further provided an NOI encoding a protein that kills mononuclear phagocytes.

69. (new) A method for selectively destroying a mononuclear phagocyte comprising:

- (i) providing a mononuclear phagocyte according to claim 68; and (ii)

mononuclear phagocyte is selectively destroyed after expression of the cytotoxic, hypoxially and/or ischaemically and/or stress activated agent at the target hypoxic and/or ischaemic and/or stress site.

70. (new) A method for targeting a mononuclear phagocyte to hypoxic and/or ischaemic and/or stress sites comprising;

- (i) providing a mononuclear phagocyte as defined in claim 51; and
- (ii) allowing said mononuclear phagocyte to migrate under conditions that support migration to a hypoxic and/or ischaemic and/or stress site either *in vitro* or *in vivo*.

71. (new) A method for treating a condition associated with hypoxic and/or ischaemic and/or stress state comprising administering to an individual to be treated a mononuclear phagocyte according to claim 51.

72. (new) A method for treating a condition associated with a hypoxic and/or ischaemic and/or stress state comprising;

- (i) withdrawing blood and/or serum from an individual to be treated;
- (ii) treating said blood and/or serum *in vitro* with a mononuclear phagocyte according to claim 51; and
- (iii) re-injecting said treated blood and/or serum into the individual either systemically or directly into a hypoxic and/or ischaemic and/or stress area.

73. (new) A delivery system for targeting a mononuclear phagocyte according to

and/or ischaemic and/or stress associated condition is a tumour associated condition.

75. (new) A construct comprising at least one hypoxia and/or ischaemic and/or stress regulatable element operably linked to at least one NOI wherein the construct is coupled to a binding agent that is capable of binding to a cell surface element of a mononuclear phagocyte.

76. (new) A construct according to claim 75 wherein the hypoxia and/or ischaemic and/or stress regulatable element is an HRE element.

77. (new) A construct according to claim 75 or claim 76 wherein the binding agent comprises a ligand adapted to bind to the cell surface element, preferably wherein the ligand is a mannosylated poly - L —lysine.

78. (new) A construct according to claim 75 or claim 76 wherein the binding agent comprises a viral vector for internalising the hypoxia and/or ischaemic and/or stress regulatable element into a mononuclear phagocyte.

79. (new) A construct according to claim 78 wherein the viral vector is selected from the group consisting of an adenoviral vector and a lentiviral vector.

80. (new) A method for internalising a hypoxia and/or ischaemic and/or stress regulatable element into a mononuclear phagocyte wherein the method comprises:

- (i) providing a mononuclear phagocyte; and
- (ii) exposing the mononuclear phagocyte to a construct as defined in any one of claims 75 or 76 under conditions sufficient to internalise the construct into the

ischaemic and/or stress state comprising administering to an individual to be treated a construct according to any one of claims 75 or 76.

82. (new) A method for treating a condition associated with a hypoxic and/or ischaemic and/or stress state comprising;

- (i) withdrawing blood and/or serum from an individual to be treated,
- (ii) treating said blood and/or serum *in vitro* with a construct according to any one of claims 75 or 76; and

re-injecting said treated blood and/or serum into the individual either systemically or directly into a hypoxic and/or ischaemic and/or stress area.

83. (new) A construct according to any one of claims 75 or 76 wherein the hypoxic and/or ischaemic and/or stress associated condition is a tumour associated condition.

84. (new) A pharmaceutical composition comprising a mononuclear phagocyte according to claim 51 optionally admixed with a pharmaceutically acceptable diluent, excipient or carrier.

85. (new) A pharmaceutical composition comprising a construct according to any one of claims 75 or 76 optionally admixed with a pharmaceutically acceptable diluent, excipient or carrier.

86. (new) A mononuclear phagocyte comprising an NOI encoding a p450 enzyme wherein the NOI has been internalised into the mononuclear phagocyte by an internalisation vector and wherein the NOI encoding the p450 enzyme is operably linked to